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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/731,375	12/08/2003	Philip J. Barr	368292001700	4368

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EXAMINER	
KIM, JENNIFER M	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
07/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/731,375	BARR ET AL.	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5,8,11 and 13-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,8,11 and 13-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/15/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submission filed on June 15, 2007 has been entered.

Action Summary

The rejection of claims 5, 8, 11, 13 and 15-20 under 35 U.S.C. 103(a) as being unpatentable over Avidano et al. (Head and Neck Surgery, Oct., 1998) of record in view of Lezdey et al. (U.S.Patent No. 6,174,859 B1) is being maintained for the reasons stated in the previous Office Action.

The rejection of claims 14, 20 and 21 under 35 U.S.C. 103(a) as being unpatentable over Avidano et al. (Head and Neck Surgery, Oct., 1998) of record in view of Lezdey et al. (U.S.Patent No. 6,174,859 B1) as applied to claims 5, 8, 11 and 13 above, and further in view of Brake et al. (U.S.Patent No. 4,752,576) of record is being maintained for the reasons stated in the previous Office Action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 5, 8, 11, 13 and 15-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Avidano et al. (Head and Neck Surgery, Oct., 1998) of record in view of Lezdey et al. (U.S.Patent No. 6,174,859 B1) of record.

Avidano et al. teach otorrhea samples were collected from **human patients with otitis media** and a **perforated tympanic membrane** and the samples were treated with ilomostat plus **alpha1-antitrypsin** in *vitro*. (abstract). A statistically significant ($p<0.05$) decrease in protease activity against **Pseudomonas** was seen **with the addition of alpha 1-antitrypsin** or **ilomostat plus alpha1-antitrypsin** but not with ilomostat alone. (see Fig. 1, page 348). Avidano et al. teach that chronic otitis media is a common problem associated with a nonintact tympanic membrane involving **pseudomonas**. (abstract). Avidano et al. teach that the concentration of ilomostat was prepared with 800ug/ml (0.8mg/ml) in a vehicle and the alpha 1-antitrypsin was prepared at a concentration of 100ug/ml (0.1mg/ml). These amounts are within the nontoxic amounts claimed by the Applicants set forth in claims 18 and 19.

Avidano et al. do not teach the actual *vivo* treatment with an effective *vivo* amount set forth in claim 13 and further comprising steroid set forth in claim 5.

Lezdey et al. teaches composition comprising **alpha 1-antitrypsin** and **steroid** compound for the **patients (vivo)** suffering from **ear infections** caused by **pseudomonas**. (abstract, claims 1-16, particularly claims 1 and 16, Examples 1-8 particularly 7 and 8). Lezdey et al. teaches the effective amount of alpha 1-antitrypsin to be administered in vivo from about **0.1 to 20 mg per 1ml of solution**.

It would have been obvious to one of ordinary skill in the art to employ the teaching of Avidano et al. to a patient (vivo) suffering form otitis media and a perforated tympanic membrane by administering effective amount of alpha one-antitrypsin without significant ototoxicity because Avidano et al. obtained statistically significant decrease in protease activity against Pseudomonas in the sample collected from human who actually had otitis media and because the effective therapeutic amount of alpha one-antitrypsin for the treatment of ear infection caused by pseudomonas is well known by Lezdey et al. One would have been motivated to employ the successful teaching of Avidano et al. in vitro data comprising human sample of otitis media having perforated tympanic membrane to a patient actually suffering from the such condition in order to achieve an expected benefit of actual effect in vivo. One would have been motivated to make such modification because Avidano et al. obtained statistically significant decrease in protease activity in sample collected from human with otitis media. Further, to employ the result obtained from the actual human sample taught by Avidano et al. and modify further in vivo would be next logical step. Moreover, to further incorporate an effective amount of steroid in the obvious method, such is obvious because Lezdey et al. teaches that steroids are routinely combined with **alpha 1-antitrypsin** for the **patients (vivo)** suffering from **ear infections** caused by **pseudomonas**. One would have been motivated to combine steroid with alpha one-antitrypsin in order to achieve at least an additive effect in treatment of ear injection involved with pseudomonas with the routine combination therapy well known by Lezdey et al. With regard to the cause of perforated tympanic membrane due to tympanostomy set forth in claim 8, such is

obvious because the alpha one-antitrypsin is effective for the treatment of otitis media with perforated tympanic membrane regardless of its etiology. Absent any evidence to contrary, there would have been a reasonable expectation of successfully treating an individual having otitis media and a perforated tympanic membrane with alpha one-antitrypsin well known by Avidano et al. having significant antiprotease activity in human otitis media sample.

Claims 14, 20 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Avidano et al. (Head and Neck Surgery, Oct., 1998) of record in view of Lezdey et al. (U.S.Patent No. 6,174,859 B1) of record as applied to claims 5, 8, 11 and 13 above, and further in view of Brake et al. (U.S.Patent No. 4,752,576) of record.

The teachings of Avidano et al, Lezdey et al as applied as before.

Avidano et al, and Lezdey et al. do not teach the source of the alpha-1 antitrypsin is yeast-expressed rAAT set forth in claim 14 and the result of the treatment set forth in claims 20 and 21.

Brake et al. teach a method for producing alpha1-antitrypsin (AAT) by recombinant methods from yeast. This method provides high level production of the protein. (abstract, column 1, lines 59-68, column 2, lines 7-15).

It would have been obvious to one of ordinary skill in the art to employ the recombinant AAT obtained by yeast –expressed rAAT in Avidano et al as modified by Lezdey et al. because Brake et al. teach the method of producing alpha1-antitrypsin (ATT) by recombinant methods in yeast provides high level production of the protein. One would have been motivated to employ yeast-expressed rAAT in Avidano et al's

method modified by Lezdey et al. because the method of producing the alpha1-antitrypsin by yeast method provided high level of production and is well known and readily available by Brake et al. Further, to optimize different signs and symptoms to measure and detect an ototoxicity of a given treatment involving otitis media is well within the knowledge of the skilled artisan. Once the patient is being treated with a particular therapy involving a particular regimen, it is well within the knowledge of skilled artisan to routinely measure and evaluate the patient's condition and detect signs and symptoms of toxicity.

Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

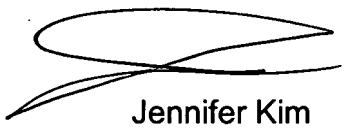
None of the claims are allowed.

Information Disclosure Statement

The Information Disclosure Statement filed June 15, 2007 has been reviewed and considered, see the enclosed copy of PTO FORM 1449.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Jennifer Kim
Patent Examiner
Art Unit 1617

Jmk
July 3, 2007